

Ernst Rüdin (1874–1952) and His Genealogic-Demographic Department in Munich (1917–1986): An Introduction to Their Family Studies of Schizophrenia

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This historical review introduces a series of papers abstracting, reanalyzing and commenting upon family studies of schizophrenia conducted by Ernst Rüdin and his genealogic-demographic department in Munich. These studies, which pioneered many of the methods still critical to psychiatric genetics, are little known in the anglophonic world. Starting with a study of schizophrenia in siblings, members of the Rüdin school expanded to study a wide range of relationships (including grandchildren and nieces/nephews) and disorders (including affective illness, obsessive-compulsive disorder, epilepsy and personality disorders). They examined many methodologic issues in psychiatric genetics including i) ascertainment correction, ii) anticipation, iii) age correction, iv) assortative mating, v) reduced fertility, vi) spectrum disorders, and vii) familial transmission of age at onset. After the rise of Hitler in Germany, Rüdin and his institute became involved in the eugenic policies of the Nazis, raising important questions about possible political abuse of scientific findings in general and those from the field of psychiatric genetics in particular. © 1996 Wiley-Liss, Inc.

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INTRODUCTION

Psychiatry as a discipline has too often been characterized by many speculations based on few facts. There-

fore, the few areas of research in which we have a large corpus of empirical data are to be especially valued. Such is the case with studies of the familial aggregation of schizophrenia. In fact, here we might say that we have the opposite problem—a great many facts the meaning of which are not completely clear.

As we hope to convey to the reader, family studies of schizophrenia is an area in which psychiatry has produced a truly impressive body of research. And yet, despite renewed interest in psychiatric genetics, fueled by developments in diagnosis, statistical genetics, and molecular biology, a number of research psychiatrists in the anglophonic world remain uninformed about important details of the extensive continental tradition of psychiatric genetics.

Why this gap in knowledge? We would suggest two reasons: a language barrier and a rather virulent form of “presentism”: (the tendency to value only recent endeavors and neglect the work of previous eras). As the generation of psychiatrists trained in central Europe has aged and died in the US and UK and been replaced by a new generation of functionally monoglot psychiatrists, a veil has fallen over much of 20th century psychiatry produced before World War II, the time in which Germany was the world center of psychiatric research. The presentism, so common in science, comes in a variety of forms. One might be termed “methodologic,” in which all early family studies of schizophrenia are dismissed with a phrase such as “they weren’t double-blind.” A related form of presentism, particularly suffused with hubris, might be termed “diagnostic presentism.” From this perspective, all early family studies can be dismissed because they “didn’t use operationalized criteria” or “used broad pre-DSM-III concepts of schizophrenia.”

This article is to serve as an introduction to a series of papers to follow that will review the major family studies of schizophrenia performed by individuals associated with the “school” of Psychiatric Genetics established by Ernst Rüdin in Munich. If time and resources allow, we may expand our efforts to include other family studies of schizophrenia published in European languages and even English language monographs now rarely cited and even more rarely read.

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In reviewing the motivation for our efforts, we can articulate four inter-related goals. The first and most straightforward is to present the major results of the many family studies of schizophrenia. This alone is not sufficient motivation for our work, because it has been thoroughly done by one of us in tabular form [Zerbin-Rüdin, 1967] and because other aspects of this work have been reviewed previously [Slater, 1971; Rosenthal, 1970; Fuller and Thompson, 1978]. Second, we wanted to review a certain set of core methodologic issues for each study. These would include, where available, the diagnostic approach to schizophrenia and related conditions, the method of ascertainment of probands, the assessment of relatives, and the method of age correction. Third, we wished to convey a "sense" of what these studies were like to conduct and analyze. While it was clear to us that we were not writing a history of psychiatric genetics in the 20th century, a full appreciation of this corpus of knowledge cannot be obtained without some idea of the context in which these studies occurred. Finally, we wished to present a synthesis of this work that would move beyond the tabular summaries of morbid risks. This would include "side lights" such as the large, but relatively unrecognized, body of information about what we would now call "schizophrenia spectrum" disorders in relatives of schizophrenics.

It became obvious to us early in this process that these goals could not be met with any series of tables of summarized results. Therefore, we settled on the format of a series of "abstracts/analyses" of each study, taken one at a time. While we recognize that this format may strain the patience of some readers, we hope it will also provide a richness of data and description that would have been unobtainable in any other format.

THE BEGINNINGS OF THE PSYCHIATRIC GENETICS SCHOOL OF RÜDIN

"Genetic" investigations of psychiatric disorders in Europe in the 19th and early 20th century examined selected large families with many affected members or concordant twin pairs. Rüdin was the first to examine relatives of a large scale series of unselected probands. Having been in close contact with Weinberg, the leading German statistical geneticist of that era, probably from around 1910, Rüdin was aware of advances Weinberg had made in the problems of correcting for both the method of selection of probands (ascertainment) and the variable ages of relatives at evaluation (age correction) [Weinberg, 1903, 1908]. Rüdin was the first to apply these new techniques to psychiatric genetic studies. For his first famous study of schizophrenia [1916], Rüdin ascertained all patients with the diagnosis of schizophrenia from the admission registries of the Munich psychiatric hospitals from their opening until about 1913. He attempted to confirm the diagnoses from the medical records and, if the patients were still living, by personal examination. He used the diagnostic concept of Kraepelin, who was then the head of the Psychiatric Hospital of the University of Munich and his superior. He then obtained the names, addresses, place and date of birth, date of death (if applicable), and mar-

ital status on all the first degree relatives of these probands. Complete ascertainment of this information was relatively easy for Rüdin, as in Germany every citizen was obliged to register his place of abode with the local police, government, or community office. Children who died in early infancy were ascertained from the local parish registers.

Family members who were still alive and residing in Bavaria were visited whenever possible. Additional information was obtained from family records (which were often quite extensive and kept in a "family book" or the family bible), hospital records, priests, teachers, files of public health departments, legal records kept on inheritances and property, divorce, guardianship, prisons, police law courts, or military service. Moreover, Bavaria at that time had a largely rural population, living in villages or small towns where everybody knew everybody.

Rüdin visited all the families himself, mostly in his spare time, as he was fully occupied by his clinical work in the Psychiatric University Hospital of Munich. Railway lines were available for some places in the country where visits had to be made. However, Rüdin often had to ride a bicycle. A secretary at the University Hospital helped with writing the letters to families and authorities. Contacts by telephone were not possible, as only a few citizens, and no farmers, would then have owned a telephone. This general procedure of obtaining information on relatives was followed by all studies from Rüdin's institute.

DEVELOPMENT OF RÜDIN'S DEPARTMENT

In 1916, Rüdin was an assistant professor at the Munich Psychiatric University Hospital. In 1917, Emil Kraepelin founded the "Deutsche Forschungsanstalt für Psychiatrie" (The German Research Institute for Psychiatry), which included, among other departments, the "Genealogic-Demographic Department" headed by Rüdin. In the beginning, however, this "department" really existed only on paper. In the early 1920s, a private flat was hired (the other departments, too, were scattered in rooms and flats), and in 1924 two assistants, B. Schulz and H. Luxenburger, were engaged. They became Rüdin's most effective and successful co-workers and stayed with him until 1945 and 1942, respectively. Guests arrived, and one of them recalled that the space was so limited that he had to write his manuscript in the kitchen, using the stove as a writing table!

In 1928, the Deutsche Forschungsanstalt received a house of its own, which is still in use. The Genealogic-Demographic Department obtained sufficient space, expanded, and employed more assistants and psychiatrists from all over Germany and from other European countries, who came as guests to learn Rüdin's methods. These guests included many of the major figures of the next generation in psychiatric genetics including Kallmann, Slater, Strömberg, Sjögren, and Essen-Möller.

All of them adapted the basic research approach of Rüdin, though in the course of time available methods were refined and new ones introduced. The working conditions improved significantly from the time Rüdin had conducted his first study of schizophrenia. The assistants held fulltime jobs as research workers, and in

most instances the salaries of the guests were paid by their home institutions. Everyone was free to use all of the facilities of the department, especially the writing office, where about 20 young women worked, typing the letters to families and authorities, sorting the replies to these letters, and working out the pedigrees. The permanent assistants had a personal secretary at their disposal. Visits were made using public transportation and a lot of walking. From the middle of the 1930s, a "research car" was available for the assistants to share.

DIAGNOSTIC APPROACH

The diagnostic approach to schizophrenia adopted in Rüdin's department was strict and followed the teachings of Kraepelin. In principle, the same criteria were applied to affected probands and relatives. Cases of schizophrenia were accepted as certain only when seen personally, hospitalized, seen by a medical colleague, or described beyond doubt by a priest, teacher, or several relatives. In practice, however, the diagnoses of deceased relatives, especially of the parental generation, might not always have fulfilled these requirements. On the other hand, cases of schizophrenia or suicide might have been missed, again especially in the parental generation.

Guests from Switzerland or the Scandinavian countries, though adopting Rüdin's biostatistical methods, sometimes used different diagnostic concepts. This, however, will be explained when we abstract these specific papers.

Operationalized criteria, as the term is currently used, did not exist. Furthermore, diagnoses were not made "blindly," but with knowledge of the diagnosis of the proband. Because the importance of avoiding bias was appreciated, substantial care was taken to insure that the psychiatric diagnosis in a relative was not influenced by any prior available knowledge about the psychiatric status of the proband or other family members. Similarly, all attempts were made to have the diagnosis of the proband made without regard to the presence or absence of psychiatric illness in his or her family. Moreover, sometimes diagnoses of the proband were checked by a psychiatrist "blind" to the family data obtained by other investigators in the department.

METHODS

In general, one investigator was responsible for a given study and performed all visits and interviews. Sometimes, the investigator would approach Rüdin with the request to come and study with him and learn his methods. In that case, Rüdin would usually work out the plan and purpose of the study, provide the money, assure access to the various authorities and files, and give advice when asked for it. In general, however, individuals were encouraged to think for themselves and minor problems were discussed with B. Schulz. At other times, such as in the case of Kallmann, the investigator approached Rüdin with a specific research plan, often to be carried out at the home institution of the investigator. Rüdin would then give advice and, when necessary, supervision on this project, often with other senior colleagues such as B. Schulz. The fa-

vorite place for scientific, or other discussions, as well as for little parties, was the canteen where the scientific members of the department met together for lunch and coffee. A lecture theatre was also available for more formal presentations.

Methods of Ascertainment

Early on, Rüdin had appreciated the necessity of studying an unselected series of probands from various hospitals and clinics, of attempting to obtain information on *all* relatives, and of examining, personally, as many relatives as possible. All papers indicate how many cases of schizophrenia were collected first and how many were eliminated after attempting confirmation of the diagnosis. Most, but not all, papers also state how many persons were eliminated "for other reasons," chiefly refusal to cooperate or lack of information. Very few of the papers indicate how many relatives were visited personally, assessed by letter, or evaluated solely on the basis of "secondary" information. A file was established for every proband which contained a pedigree and all information about both the proband and his or her relatives.

Methodologic Issues

Impressed by the recent rediscovery of the Mendelian laws, Rüdin hoped that by using the correct genetic methods, he would be able to uncover the proper Mendelian ratios for schizophrenia. This hope was not fulfilled so that he had to resort to the calculation of empirical risk figures. All classes of relatives, including the three different kinds of first-degree relatives (parents, sibs, and offspring), were treated separately. In each class, frequency tables for, e.g., sex, living or deceased at time of follow-up, age at observation time and onset of illness, birth number, profession, urban or rural birth, or place of living were worked by hand, placing tally marks on large sheets of paper. When obtaining age-corrected risks, Weinberg's abridged method was most often used, but other methods such as the Diem-Koller method or Bernstein's *a priori* method were also tested [Schulz, 1936]. When Strömberg's more precise method of age correction was published in 1935 (Strömberg, 1935), it was sometimes applied instead of or in addition to the Weinberg method.

Methodological problems were given great attention, and most of the early papers started with methodological considerations. Several papers, especially by Schulz [1934, 1936, 1938] and Luxenburger [1928a, 1931, 1934, 1940], dealt with methodological problems exclusively.

Control Groups

In the first family study conducted by Rüdin, he started from schizophrenic probands and studied their siblings and parents. He also examined the frequency of illness in the offspring of various combinations of parental matings seeking for mendelian ratios. Because his initial goal was to find the mendelian mode of transmission of schizophrenia, rather than merely to document familial aggregation, a control group was not seen as necessary.

However, consistent mendelian ratios did not emerge in any group. Therefore, Rüdin had to be satisfied with empirical risk figures and soon realized the need to compare these obviously increased risks with figures derived from the general population.

He therefore suggested obtaining control groups (called "figures for comparison" at that time) by examining families of nonpsychiatric probands. The first study of this kind, the purpose of which was to calculate the prevalence or morbid risk of psychiatric disorders in "control populations," was performed by Schulz [1927] and examined families of the spouses of patients with cerebral sclerosis (arteriosclerosis of the brain). Luxenburger's study of the families of the spouses of patients with general (syphilitic) paralysis followed in 1928 [Luxenburger, 1928a]. Other authors collected random samples of probands from the official birth registers [Klemperer, 1933] or from census data [Brugger, 1938]. Thus, the controls came from the same Bavarian population as the schizophrenic probands, but they were not formally matched to any group of schizophrenic probands.

Topics Dealt With at the Genealogic-Demographic Department

To confirm the initially obtained empirical risk figures, Rüdin and his colleagues sought to enlarge their series of probands from Bavaria, and complement them with proband series obtained from elsewhere in Germany and from other European countries. Their studies were not restricted to first-degree relatives, but also examined second-degree relatives, particularly grandchildren [Juda, 1928; Oppler, 1932; Kallmann, 1938] and nieces/nephews [Schulz, 1926; Walker, 1929; Konstantinu, 1930; Kallmann, 1938]. Various parental matings were ascertained: schizophrenic x normal; schizophrenic x schizophrenic [Schulz, 1940a]; schizophrenic x otherwise psychotic [Schulz, 1940b]; and normal x normal, but each spouse having at least one schizophrenic relative [Schulz, 1939]; and then the offspring were studied. In contrast, Rüdin in 1916 set out from schizophrenic probands, studied sibs and parents, and then subdivided the sibships according to the parental matings found [Rüdin, 1916].

Other studies dealt with i) special forms of schizophrenia such as the catatonic [Knoll, 1954], ii) the degree to which the age of onset to schizophrenia was inherited [Schulz, 1940c], iii) anticipation [Schulz, 1940c] (the tendency for age at onset to become younger in succeeding generations), iv) assortative mating [Egger, 1942; Früh, 1943], and v) reduced marital rate and diminished fertility associated with mental illness [Essen-Möller, 1935]. Several methodologic papers examined issues in the calculation and interpretation of empirical risk figures, emphasizing their importance for genetic counselling [Luxenburger, 1928b, 1930b, 1936, 1940, Schulz, 1937]. The term "Empirische Erbprognose" ("empirical heredity prognosis") was coined. Twin studies were also done, but they are not to be discussed here.

Rüdin and his colleagues were, from an early time, aware of the problem of what would now be termed the

boundaries of the schizophrenia spectrum. Studies examined, from a familial perspective, the relationship between schizophrenia and i) psychoses other than schizophrenia (e.g., paranoia [Lange, 1924]), manic-depressive illness [Slater, 1936, 1938], atypical psychoses [Schulz and Leonhard, 1940], ii) alcoholism [Brugger, 1934], iii) mental retardation [Juda, 1937], iv) abnormal personality ("psychopathy") [Berlit, 1931; Riedel, 1937], and v) tuberculosis [Schulz, 1933; Kallmann, 1938]. Their main interest, however, was in one form of abnormal personality called most commonly schizoidia or schizoid personality. In the tables of many papers, a separate column of figures was presented for "schizoid personality." However, everybody in Rüdin's group agreed that this personality syndrome was difficult to recognize. Although it was generally accepted that schizophrenia and schizoidia were related in some way, there was also wide acceptance of the fact that some individuals with a schizoid personality carried little or no genetic endowment for schizophrenia and some schizophrenic patients did not have a premorbid schizoid personality.

Disorders Other Than Schizophrenia

Although beginning with schizophrenia, in the course of time, research in Rüdin's group was extended to manic-depressive illness [Banse, 1929; Slater, 1936, 1938], epilepsy [Conrad, 1937], mental retardation [Juda, 1937], abnormal personality [Berlit, 1931; Riedel, 1937], obsessive-compulsive disorder [Luxenburger, 1930a], criminality [Stumpff, 1933], Huntington's chorea [Entres, 1921], and multiple sclerosis [Thums, 1939]. Research was also conducted on physical disorders that were suspected of being associated with mental disorders, including inborn malformations (with schizophrenia and mental retardation) [Idelberger, 1939] or diabetes (with depression) [Then Bergh, 1939].

Quite early, Rüdin began a study of the putative connection between "genius and madness." As he was reluctant to believe that high levels of ingenuity and creativity required "a dash of madness," he decided to study this problem systematically. Later, he delegated the project to A. Juda, who in contrast also studied mental retardation. The inquiries were carried on over decades, and when at last the manuscript was completed, its appearance in print was thwarted once more by war—World War II. An abridged version appeared in 1953, edited after Juda's death by B. Schulz [Juda, 1953]. This study found a modestly increased risk for psychiatric illness in the gifted probands (which appeared to vary by occupation, with schizophrenia being increased among artists and affective illness among scientists). Families of these probands had both a slightly increased risk for major psychiatric illness and an excess of highly gifted persons.

The Role of Rüdin in the Third Reich

The relationship between Rüdin and his institute and the racial and eugenic policies of the Nazi party after it came to power in Germany is an historically important subject, not least because it raises significant

questions about the possible misuse and abuse of findings from the field of psychiatric genetics. Because the focus of this article and the subsequent reviews is on the scientific and methodologic work of the Rüdin school, we will not, however, explore these important questions here. They have been examined in detail in both a recently published biography of Rüdin [Weber, 1993] and a series of relevant documents compiled by E.Z.R. [Zerbin-Rüdin, 1986].

Concluding History of Rüdin's Department

During World War II, the assistants in Rüdin's department served in the German army. The building housing the department was heavily damaged by Allied bombing. Because of the widespread and profound abuses of genetics by the Nazi Regime, post-war public opinion in Germany made further work in psychiatric genetics very difficult. After the war, Rüdin's Institute, reorganized as a department, was continued by B. Schulz, E. Zerbin-Rüdin [Rüdin's daughter (1921-)], one secretary, and some students completing their doctoral dissertations. After Schulz's death in 1958, the department became a working group headed by Zerbin-Rüdin. Upon her retirement in 1986, the department was formally disbanded.

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